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# TRANSMITTAL FORM

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Application Number	09/844,935
Filing Date	04/27/2001
First Named Inventor	Alexander Munishkin, et al.
Group Art Unit	1634
Examiner Name	Arun K. CHAKRABARTI
Attorney Docket Number	30318-110CON

Total Number of Pages in This Submission

## ENCLOSURES (check all that apply)

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| <input type="checkbox"/> Fee Transmittal Form<br><input type="checkbox"/> Fee Attached<br><input checked="" type="checkbox"/> Amendment / Reply<br><input type="checkbox"/> After Final<br><input type="checkbox"/> Affidavits/declaration(s)<br><input type="checkbox"/> Extension of Time Request<br><input type="checkbox"/> Express Abandonment Request<br><input type="checkbox"/> Information Disclosure Statement<br><input type="checkbox"/> Certified Copy of Priority Document(s)<br><input type="checkbox"/> Response to Missing Parts/ Incomplete Application<br><input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53 | <input type="checkbox"/> Assignment Papers (for an Application)<br><input type="checkbox"/> Drawing(s)<br><input type="checkbox"/> Licensing-related Papers<br><input type="checkbox"/> Petition<br><input type="checkbox"/> Petition to Convert to a Provisional Application<br><input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address<br><input type="checkbox"/> Terminal Disclaimer<br><input type="checkbox"/> Request for Refund<br><input type="checkbox"/> CD, Number of CD(s) _____ | <input type="checkbox"/> After Allowance Communication to Group<br><input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences<br><input type="checkbox"/> Appeal Communication to Group (Appeal Notice, Brief, Reply Brief)<br><input type="checkbox"/> Proprietary Information<br><input type="checkbox"/> Status Letter<br><input checked="" type="checkbox"/> Other Enclosure(s) (please identify below):<br>Post Card |
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Remarks

## SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name: Stephen J. Gaudet  
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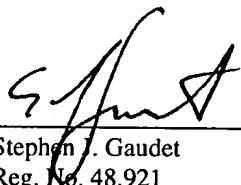
<b>Applicant:</b>	Munishkin and Grossman	)	
		)	
<b>Serial No.:</b>	09/844,935	)	
		)	
<b>Filed:</b>	April 27, 2001	)	<b>Art Unit:</b> 1634
		)	<b>Examiner:</b> Chakrabarti
<b>Title:</b>	Compositions, Methods,	)	
	Kits, and Apparatus for	)	
	Determining the Presence or	)	
	Absence of Target Molecules	)	
		)	
<b>Docket No.:</b>	30318-110CON	)	
		)	

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By:   
Stephen J. Gaudet  
Reg. No. 48,921  
Attorney for Applicants

**REPLY**

Sir:

In reply to the Office Action dated December 23, 2002, Applicants file the following response.

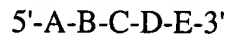
Remarks

**Rejection of claims 1-5 and 7 are rejected under 35 USC 102(b)**

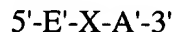
Claims 1-5 and 7 are rejected under 35 USC 102(b) as being anticipated by Marsh et al. (Nucleic Acids Research (1988) 16(3), pp. 981-995).

The Examiner states that Marsh et al. teaches a method of determining the presence or absence of a target molecule comprising the steps of

[a] (i) providing a first RNA molecule having the formula:



wherein, A is a section of the RNA molecule ... with another sequence, E, replicated by an RNA replicase, the letter "B" denotes a section of RNA ... with another sequence D, binds the target molecule... "C" denotes a section of the RNA molecule ... "D" denotes a section of the RNA molecule... and (ii) a second RNA molecule having the formula:



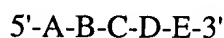
[b] imposing binding conditions on a sample potentially containing target molecules in the presence of the first RNA molecule ...

[c] imposing RNA replicase reaction conditions on [b] ...

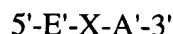
[d] monitoring a second modified sample for the presence of the second RNA molecule ...

Section 102 of Title 35 provides the novelty requirements for patentability. In order for a prior art reference to anticipate a claim it must teach each and every element of that claim. M.P.E.P. §2131. The Court of Appeals for the Federal Circuit states:"[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628 (CAFC, 1987).

The instant invention claims a composition for determining the presence or absence of a target molecule comprising a first RNA molecule that binds the target molecule of interest. The first RNA molecule has the formula of:



wherein A is a section of the RNA molecule together with section E is replicated by a replicase; "B" denotes a section of RNA sequence together with "D" that actually binds the target molecule under proper binding conditions; "C" is a section of RNA that is capable of preventing replication. Once the target molecule is bound by sections "B" and "D" a replicase acts upon the complex to form a second RNA molecule having the following formula:



wherein, E' is the complement to E, and A' is the complement to A, and "X" denotes the complement of parts of "B" and "D" that can be replicated, or the direct bond between sections E' and A'.

Contrary to the Examiner's position, Marsh does not anticipate the present invention as claimed. First, Marsh does not recite an RNA molecule having the formula 5'-A-B-C-D-E-3'. For example, there is no analog to RNA sections "B" and "D" as claimed by Applicants in the Marsh disclosure. Recall, these sections in Applicants' invention form secondary structure and are employed to bind a target molecule, specifically a protein target. Marsh fails to recite any analogous RNA regions. Further, unlike the presently claimed invention, Marsh fails to disclose a paired RNA molecule composition.

Moreover, section "C" as claimed by Applicants is completely absent from Marsh, as adroitly pointed out by the Examiner on page 5 of the *Office Action* dated 12/23/02. In the presently claimed invention, section "C" is a stretch of RNA that can be used to inhibit replicase activity. The Examiner points out that Marsh has an analogous section that serves as a non-base-paired spacer to facilitate access of the replicase to the promoter. This simply is not equivalent to the claimed invention. Applicants in the specification characterizes section "C" as comprising "stop" sequences. This is very

different than just a spacer element. Therefore, Marsh fails to recite an equivalent to sequence "C" of Applicants' presently claimed invention.

Further, in order to arrive at the claim's second RNA molecule, a target (protein) molecule has to bind with sections "B" and "D" of the first molecule, then replicase activity takes place. There is no analogous disclosure to be found in Marsh et al.

Marsh fails to anticipate Applicants' claimed invention based on the "each and every element" criteria established by the Federal Circuit. Therefore, Applicants respectfully request reconsideration and withdrawal of the present rejection.

**Rejection of claims 6 and 8 under 35 USC 103(a)**

Claims 6 and 8 are rejected under 35 USC 103(a) as being unpatentable over Marsh et al. (Nucleic Acids Res. (1988) 16(3), pp. 981-995) in view of Spiegelman (US Pat. No. 3,444,043).

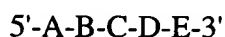
The Examiner posits that Marsh et al. teach the composition as previously described by the Examiner above. Further, that Marsh et al. [*sic*] "does not teach a composition by providing paired RNA molecules. Marsh et al. does not teach section "C" of the RNA molecule which section is capable of preventing the replication of the first molecule by the RNA replicase." *Office Action* dated 12/23/02, pg. 5.

The Examiner further characterizes Spiegelman as teaching [*sic*] "a customized preparation of RNA templates ... Spiegelman teaches section "C" of the RNA molecule which section is capable preventing the replication of the first molecule by the RNA replicase." *Office Action* dated 12/23/02, pp. 5-6.

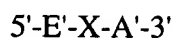
In order to establish a *prima facie* case of obviousness, "there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success.

Finally, the prior art reference (or references) must teach or suggest all of the claim limitations." M.P.E.P. §2143, see also, *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

A case of *prima facie* obviousness is not been established. The presently claimed invention claims a composition for determining the presence or absence of a target molecule comprising a first RNA molecule that binds the target molecule of interest. The first RNA molecule has the formula of:

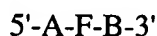


wherein A is a section of the RNA molecule together with section E is replicated by a replicase; "B" denotes a section of RNA sequence together with "D" that actually binds the target molecule under proper binding conditions; "C" is a section of RNA that is capable of preventing replication. Once the target molecule is bound by sections "B" and "D" a replicase acts upon the complex to form a second RNA molecule having the following formula:

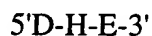


wherein, E' is the complement to E, and A' is the complement to A, and "X" denotes the complement of parts of "B" and "D" that can be replicated, or the direct bond between sections E' and A'.

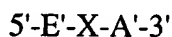
Applicants claim a composition comprising paired RNA molecules having a first RNA molecule and a second RNA molecule. The first RNA molecule binds a target molecule and has the following formula:



and a second RNA molecule that binds a target molecule having the following formula:



wherein, A and E are subject to replication by a replicase, "B" and "D" denote sections responsible for binding to a target molecule, "F" forms a hybridization product with section "H" that allows for replication of sections A and E to form a third RNA molecule having the formula:



wherein E' is the complement to E and A' is the complement to A, "X" denotes the complement of parts of "F" and "H" that can be replicated, alternatively, "X" denotes the direct bond between E' and A' and this third RNA molecule is subject to replication.

As stated above, a requirement to establish a *prima facie* case of obviousness requires that the prior art reference (or references) must teach or suggest all of the claim limitations - this requirement is simply not met by Marsh either alone or in combination with Spiegelman.

As stated above, Marsh fails to recite an RNA molecule having the formula 5'-A-B-C-D-E-3' nor does Marsh disclose an RNA having the formula 5'-A-F-B-3' nor 5'-D-H-E-3' with the attendant limitations of these formulae. For example, there is no analog to RNA sections "B" and "D" as claimed by Applicants in the Marsh disclosure. Recall, these sections in Applicants' invention form secondary structure and are employed to bind a target molecule, specifically a protein target. Marsh fails to recite any analogous RNA regions. Still another example, "F" and "H" which serve to form a hybridization product in Applicants' claimed invention is completely absent in Marsh. Further, unlike the presently claimed invention, Marsh fails to disclose a paired RNA molecule composition.

Moreover, section "C" as claimed by Applicants is completely absent from Marsh, as adroitly pointed out by the Examiner on page 5 of the *Office Action* dated 12/23/02. In the presently claimed invention, section "C" is a stretch of RNA that can be used to inhibit replicase activity. The Examiner points out that Marsh has an analogous section that serves as a non-base-paired spacer to facilitate access of the replicase to the promoter. This simply is not equivalent to that which is presently claimed. Applicants in the specification characterizes section "C" as comprising "stop" sequences. This is very different than just a spacer element. Therefore, Marsh fails to recite an equivalent to sequence "C" of Applicants' presently claimed invention.

Further, in order to arrive at the claimed second RNA molecule, a target (protein) molecule has to bind with sections "B" and "D" of the first molecule, then replicase activity takes place. There is no analogous disclosure to be found in Marsh et al.

Spiegelman fails to rectify the deficiencies of Marsh. Spiegelman fails to recite an RNA molecule having the formula 5'-A-B-C-D-E-3' nor does Spiegelman disclose an RNA having the formula 5'-A-F-B-3' nor 5'-D-H-E-3' with the attendant limitations of these formulae. For example, there is no analog to RNA sections "B" and "D" as claimed by Applicants in the Spiegelman disclosure. Recall, these sections in Applicants' invention form secondary structure and are employed to bind a target molecule, specifically a protein target. Spiegelman fails to recite any analogous RNA regions. Still another example, "F" and "H" which serve to form a hybridization product in Applicants' claimed invention is completely absent in Spiegelman. Further, unlike the presently claimed invention, Spiegelman fails to disclose a composition by providing a paired RNA molecule.

Moreover, section "C" as claimed by Applicants is completely absent from Spiegelman. In the presently claimed invention, section "C" is a stretch of RNA that is contiguous with the other sections of the RNA molecule and can be used to inhibit replicase activity. The Examiner suggests that Spiegelman has an analogous section. The "interfering compound" as Spiegelman puts it is an RNA molecule independent from the viral RNA molecule of interest. The interfering compound comprises nucleotide sequences that will interact with a replicase thus precluding replication of the independent viral RNA. This simply is not equivalent to Applicants' claimed invention. Section "C" in the presently claimed invention comprises "stop" sequences that is contiguous with the larger RNA molecule.

Further, in order to arrive at the claimed second RNA molecule, a target (protein) molecule has to bind with sections "B" and "D" of the first molecule, then replicase activity takes place. There is no analogous disclosure to be found in Spiegelman.



Marsh et al. either alone or in combination with Spiegelman does not establish a *prima facie* case of obviousness. Moreover, there is a paucity of motivation to combine these two references and even if one did, there is no reasonable expectation of success that by such combination one would arrive at the presently claimed invention. Therefore, Applicants respectfully request reconsideration and withdrawal of this rejection.

**Rejection of claim 11 under 35 USC 103(a)**

Claim 11 is rejected under 35 USC 103(a) as being unpatentable over Marsh et al. (Nucleic Acids Res. (1988) 16(3), pp. 981-995) in view of Stratagene Catalog (1988, pg. 39).

A case of *prima facie* obviousness is not established by using Marsh et al. alone or in combination with the Stratagene Catalog. For all of the reasons stated above, Marsh fails to recite each and every element of the claimed invention. The Stratagene Catalog fails to rectify the deficiencies found in Marsh. The Stratagene Catalog does disclose various kits having various reagents, however, this is wholly insufficient to establish a case of *prima facie* obviousness. In order for Stratagene to be effective in establishing a case of obviousness, it would have to rectify the deficiencies in Marsh. Moreover, there would have to be a suggestion or motivation for one to combine Stratagene with Marsh. This suggestion or motivation is completely lacking in either reference.

Applicants respectfully request reconsideration and withdrawal of the present rejection.

**Rejection of claim 12 under 35 USC 103(a)**

Claim 12 is rejected under 35 USC 103(a) as being unpatentable over Marsh et al. (Nucleic Acids Res. (1988) 16(3), pp. 981-995) in view of Spiegelman (US Pat. No. 3,444,043) further in view of Stratagene Catalog.

A case of *prima facie* obviousness is not established. The references cited by the Examiner either alone or in combination do not establish a case of *prima facie* obviousness. For the reasons stated above, neither Marsh nor Spiegelman nor the Stratagene Catalog alone or in combination establishes obviousness. The deficiencies found in the references are not rectified by the other references. Specific arguments are presented above demonstrating this fact.

Therefore, Applicants respectfully request reconsideration and withdrawal of the present rejection.

The Examiner is invited to call the undersigned attorney at (617) 854-4237 should he determine that a telephonic interview would expedite prosecution of this case.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'S. J. Gaudet', written over a horizontal line.

Stephen J. Gaudet, Ph.D.  
Attorney for Applicants  
Reg. No. 48,921

Date: 3/4/03